Access DB# 106645

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: C. Delacroix Examiner #: 71106 Date: 10/23/03
Art Unit: 1614 Phone Number 306-3227 Serial Number: 09/305,955
Mail Box and Bldg/Room Location: 2101 Results Format Preferred (circle): PAPER DISK E-MAIL
OFFICE: 2E05
If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: PLEASE see attached

Inventors (please provide full names):

Earliest Priority Filing Date:

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search method for treating pain and inflammation in a dog (Canis familiaris) by administering the compound of claim 1, Formula I. Please note the claim excludes carprofen

→ can be used to treat osteoarthritis

Please see attached claim 1

Please rush

Thank you

CM

RUSH SEARCH Approved TKaye SPE, 10-24-03

STAFF USE ONLY

Searcher:
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up:
Date Completed:
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time:

Type of Search

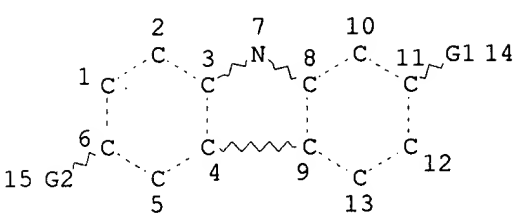
NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

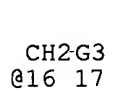
Vendors and cost where applicable

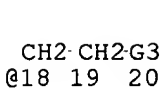
STN
Dialog
Questel/Orbit
Dr Links
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

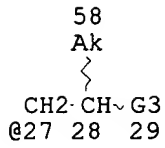
POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

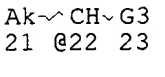
=> d que
L1 STR

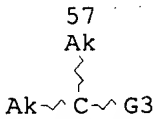


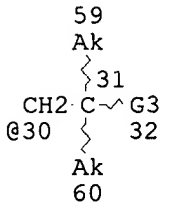


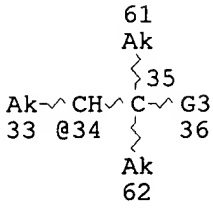


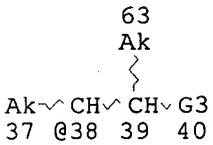


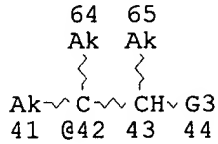


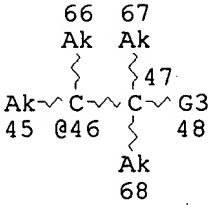


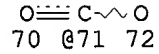












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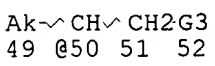
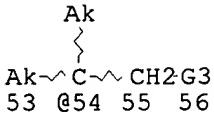
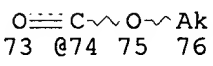
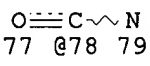
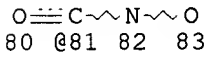
Page 1-B

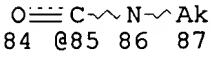


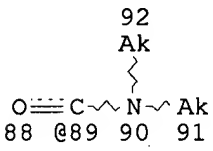


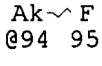












Page 2-A
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VAR G2=93/94/X/NO2
VAR G3=71/74/78/81/85/89
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CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 33

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  95

STEREO ATTRIBUTES: NONE
L3            61 SEA FILE=REGISTRY SSS FUL L1
L5         10933 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "DOG (CANIS FAMILIARIS)"+OLD,N
                 T/CT
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CARPROFEN/CN
L8            60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L7
L9            16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8(L)(BAC OR DMA OR PAC OR
                 PKT OR THU)/RL
L10            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L9
L11            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND L5
L13            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND (DOG OR CANI?)
L14            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 OR L11 OR L13
```

carprofen removed from Structure Set

Note: Stereoisomers of carprofen included in search

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=> d ibib abs hitind hitstr l14 1-8

L14  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:294811  HCAPLUS
DOCUMENT NUMBER:          139:272161
TITLE:                    Detection and identification of carprofen and its in
                          vivo metabolites in greyhound urine by capillary gas
                          chromatography-mass spectrometry
AUTHOR(S):                Dumasia, M. C.; Ginn, A.; Hyde, W.; Peterson, J.;
```

Houghton, E.
CORPORATE SOURCE: Department of Drug Metabolism, Research Division, Horseracing Forensic Laboratory, Fordham, Ely, Cambridgeshire, CB7 5WP, UK
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 788(2), 297-307
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rimadyl (carprofen) was administered orally to the racing greyhound at a dose of 2.2 mg kg-1. Following both alk. and enzymic hydrolysis, postadministration urine samples were extd. by mixed mode solid-phase extn. (SPE) cartridges to identify target analyte(s) for forensic screening and confirmatory anal. methods. The acidic isolates were derivatized as trimethylsilyl ethers (TMS) and analyzed by gas chromatog.-mass spectrometry (GC-MS). Carprofen and five phase I metabolites were identified. Pos. ion electron ionization (EI+) mass spectra of the TMS derivs. of carprofen and its metabolites show a diagnostic base peak at M+.cntdot. -117 corresponding to the loss of COO-Si-(CH3)3 group as a radical. GC-MS with pos. ion ammonia chem. ionization (CI+) of the compds. provided both derivatized mol. mass and some structural information. Deutromethylation-TMS derivatization was used to distinguish between arom. and aliph. oxidns. of carprofen. The drug is rapidly absorbed, extensively metabolized and excreted as phase II conjugates in urine. Carprofen, three arom. hydroxy and a minor N-hydroxy metabolite were detected for up to 48 h. For samples collected between 2 and 8 h after administration, the concn. of total carprofen ranged between 200 and 490 ng ml-1. The major metabolite, .alpha.-hydroxycarprofen was detected for over 72 h and therefore can also be used as a marker for the forensic screening of carprofen in greyhound urine.

CC 4-2 (Toxicology)

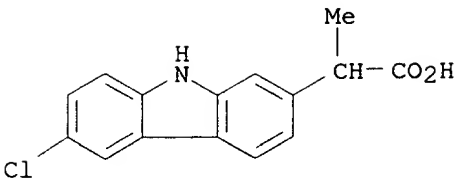
IT **Dog (Canis familiaris)**
(Greyhound; detection and identification of carprofen and its in vivo metabolites in greyhound urine by capillary gas chromatog.-mass spectrometry)

IT 53716-49-7, Carprofen **70352-29-3** 70359-62-5 76319-13-6
606977-11-1
RL: ANT (Analyte); ANST (Analytical study)
(detection and identification of carprofen and its in vivo metabolites in greyhound urine by capillary gas chromatog.-mass spectrometry)

IT **70352-29-3 606977-11-1**
RL: ANT (Analyte); ANST (Analytical study)
(detection and identification of carprofen and its in vivo metabolites in greyhound urine by capillary gas chromatog.-mass spectrometry)

RN 70352-29-3 HCAPLUS

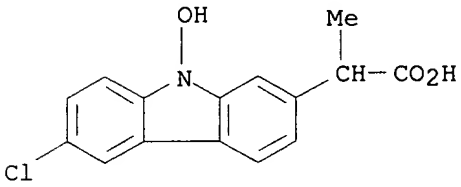
CN 9H-Carbazole-2-acetic acid, 6-chlorohydroxy-.alpha.-methyl- (9CI) (CA INDEX NAME)



Carprofen deriv.

D1— OH

RN 606977-11-1 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-9-hydroxy-.alpha.-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:754150 HCAPLUS
DOCUMENT NUMBER: 130:162885
TITLE: Evaluation of selective inhibition of **canine** cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs
AUTHOR(S): Ricketts, Anthony P.; Lundy, Kristin M.; Seibel, Scott B.
CORPORATE SOURCE: Central Research Division, Pfizer Inc, Groton, CT, 06340, USA
SOURCE: American Journal of Veterinary Research (1998), 59(11), 1441-1446
CODEN: AJVRAH; ISSN: 0002-9645
PUBLISHER: American Veterinary Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the activity of carprofen and other nonsteroidal anti-inflammatory drugs (NSAID) against isoenzymes of **canine** cyclooxygenases (COX1 and COX2). Constitutive COX1 was obtained from washed **canine** platelets, and COX2 was obtained from a **canine** macrophage-like cell line that was induced with endotoxin. Activity of carprofen and other NSAID against COX1 and COX2 was compared. Dose-response curves were plotted, and calcns. were performed to identify concns. that caused 50% inhibition (IC50 [.mu.M]) for each isoenzyme. Ratio of the COX1-to-COX2 IC50 was used as a measure of isoenzyme selectivity. Of the compds. evaluated, carprofen had the greatest selectivity for COX2. Potency of carprofen for **canine** COX2 was more than 100-fold greater than for **canine** COX1. Inhibition of

canine COX2 (IC50, 0.102 .mu.M) for the racemic mixt. of carprofen (S and R stereoisomers) was primarily attributable to the S enantiomer (IC50, 0.0371 .mu.M), which was approx. 200-fold more potent than the R enantiomer (IC50, 5.97 .mu.M). Nimesulide had the next highest selectivity for COX2 (38-fold), and tolfenamic acid and meclofenamic acid had 15-fold selectivity for COX2. The other compds. tested did not have substantial selectivity for **canine** COX2 or were more selective for **canine** COX1. Carprofen was a potent inhibitor of **canine** COX2. Of the compds. tested, carprofen had the highest selectivity for **canine** COX2. The selectivity of carprofen for **canine** COX2 may be an important factor for its use in **dogs**
.

CC 1-7 (Pharmacology)

IT Anti-inflammatory agents
(nonsteroidal; evaluation of selective inhibition of **canine** cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs)

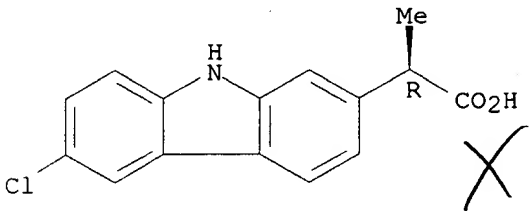
IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 644-62-2, Meclofenamic acid 13710-19-5, Tolfenamic acid 22071-15-4, Ketoprofen 38677-85-9, Flunixin 39391-18-9, Cyclooxygenase 41340-25-4, Etodolac 51803-78-2, Nimesulide **52263-83-9**, (R)-Carprofen **52263-84-0**, (S)-Carprofen 53716-49-7, Carprofen 71125-38-7, Meloxicam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(evaluation of selective inhibition of **canine** cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs)

IT **52263-83-9**, (R)-Carprofen **52263-84-0**, (S)-Carprofen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(evaluation of selective inhibition of **canine** cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs)

RN 52263-83-9 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

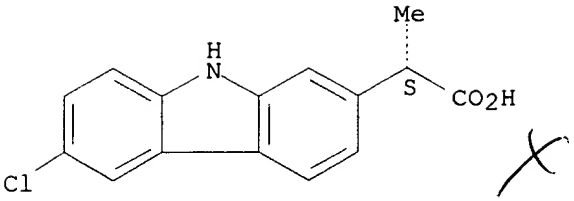


stereoisomer of Carprofen

RN 52263-84-0 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Stereoisomer of carprofen

X

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:744944 HCAPLUS
DOCUMENT NUMBER: 130:10625
TITLE: COX-2-selective carprofen and related compounds for treating pain and inflammation in **dogs**
INVENTOR(S): Lundy, Kristin Marie; Ricketts, Anthony Paul
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850033	A1	19981112	WO 1998-IB662	19980501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869321	A1	19981127	AU 1998-69321	19980501
EP 988034	A1	20000329	EP 1998-915041	19980501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9808720	A	20000711	BR 1998-8720	19980501
JP 2000513020	T2	20001003	JP 1998-547869	19980501
NZ 500183	A	20020426	NZ 1998-500183	19980501
NZ 516914	A	20030829	NZ 1998-516914	19980501
ZA 9803722	A	19991104	ZA 1998-3722	19980504
MX 9910148	A	20000228	MX 1999-10148	19991104

PRIORITY APPLN. INFO.: US 1997-45635P P 19970505
NZ 1998-500183 A1 19980501
WO 1998-IB662 W 19980501

OTHER SOURCE(S): MARPAT 130:10625

AB The invention relates to treating or preventing inflammatory processes and diseases in **dogs** assocd. with the activity of inducible cyclooxygenase-2 (COX-2), while at the same time reducing or eliminating undesirable side effects assocd. with simultaneous inhibition of the activity of constitutive cyclooxygenase-1 (COX-1) by selectively inhibiting COX-2 activity with ref. to COX-1 activity, wherein the

selectivity ratio or COX-2:COX-1 activity inhibition is at least 3:1 based on ex vivo inhibition levels measured in whole blood. The inhibitor is a member selected from the group of antiinflammatory compds. consisting essentially of salicylic acid derivs., p-aminophenol derivs., indole and indene acetic acids, heteroaryl acetic acids, arylpropionic acids, anthranilic acids, enolic acids, and alkanones; the inhibitor in particular is comprised of the (+)(S)-enantiomer of 6-chloro-.alpha.-methyl-9H-carbazole-2-acetic acid.

IC ICM A61K031-40
CC 1-7 (Pharmacology)
IT Analgesics
Anti-inflammatory agents
Dog (Canis familiaris)
Drug delivery systems
Joint, anatomical
Pharmacokinetics
Resolution (separation)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Rat (Rattus norvegicus)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and comparison with rats and humans)
IT Adrenoceptor antagonists
Anesthetics
Antibacterial agents
Antibiotics
Anticholesteremic agents
Antihypertensives
Antitumor agents
Antiviral agents
Cardiovascular agents
Cognition enhancers
Diuretics
Fungicides
Immunosuppressants
Protozoacides
Vasodilators
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Glucocorticoids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D, antagonists; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E, receptors, antagonists; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(F, receptors, antagonists; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Antihistamines
(H1; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Antihistamines
(H2; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Heart, disease
(angina pectoris, drugs; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Angiotensin receptor antagonists
(angiotensin II; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Kinins (animal hormones)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists, B1 and B2; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Platelet-activating factor receptors
Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Gout
(anti-gout agents; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Antiarteriosclerotics
(antiatherosclerotics; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Mitosis
(antimitotic agents; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Ion channel blockers
(calcium; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Drug delivery systems
(capsules; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(controlled-release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(delayed release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(elixirs; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(emulsions; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Heart, disease
(failure, drugs; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Drugs
(gastrointestinal, gastroprotective; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Drug delivery systems
(granules; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(implants; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Heart, disease
(infarction; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Drug delivery systems
(infusions, intraarterial and others; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(inhalants; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Prostaglandins
Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)
IT Drug delivery systems
(injections, i.m.; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(injections, i.v.; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(injections, s.c.; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(injections; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(liqs.; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(lozenges; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(microcapsules; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Drug delivery systems
(microparticles; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)
IT Anti-ischemic agents
(myocardial ischemia; COX-2-selective carprofen and related compds. for

treating pain and inflammation in **dogs**, and use with other agents)

IT Anti-inflammatory agents
(nonsteroidal; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Drug delivery systems
Drug delivery systems
(oral, controlled-release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(oral; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(parenterals; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(pastes; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(powders; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(solids; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(solns.; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(suppositories; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(suspensions; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(sustained-release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(tablets, delayed release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(tablets, sustained-release; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(tablets; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(tinctures; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drug delivery systems
(transdermal; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT Drugs
(uricosuric agents; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Alkaloids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Adrenoceptor antagonists
(.alpha.-; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Adrenoceptor agonists
(.alpha.2-; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT Adrenoceptor antagonists
(.beta.-; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT **52263-84-0**, (S)-Carprofen 53716-49-7, Carprofen
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT 363-24-6, PGE2 39391-18-9, Cyclooxygenase 54397-85-2, TXB2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 53-86-1, Indomethacin 61-68-7, Mefenamic acid 530-78-9, Flufenamic acid 644-62-2, Meclofenamic acid 4394-00-7, Niflumic acid 5104-49-4, Flurbiprofen 5728-52-9, Felbinac 13710-19-5, Tolfenamic acid 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22131-79-9, Alclofenac 22204-53-1, Naproxen 23981-47-7, 6-Methoxy-2-naphthylacetic acid 36322-90-4, Piroxicam 38677-85-9, Flunixin 41340-25-4, Etodolac 51803-78-2, Nimesulide **52263-83-9**, (R)-Carprofen 71109-09-6, Vedaprofen 71125-38-7, Meloxicam 120210-48-2, Tenidap 123653-11-2, NS-398 135202-79-8, Ilonidap
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and comparative inhibition of COX-1 and -2 by carprofen and other NSAIDs)

IT 52-67-5, Penicillamine 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 59-05-2, Methotrexate 64-86-8, Colchicine 118-42-3, Hydroxychloroquine 315-30-0, Allopurinol 446-86-6, Azathioprine 865-21-4, Vinblastine 3562-84-3, Benzbromarone 7440-57-5D, Gold, aurothio derivs., biological studies 59865-13-3, Cyclosporine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT 9002-17-9, Xanthine oxidase 9015-82-1 9015-94-5, Renin, biological studies 9028-35-7, HMG-CoA reductase 57576-52-0, Thromboxane A2 71160-24-2, LTB4 72025-60-6, LTC4 73836-78-9, LTD4 75715-89-8, LTE4 80619-02-9, 5-Lipoxygenase 82391-43-3, 12-Lipoxygenase 82707-54-8,

Neutral endopeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump inhibitors; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT 35121-78-9, Prostaglandin I2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptors, antagonists; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

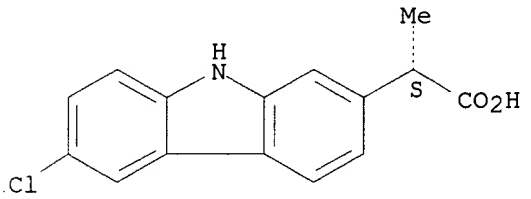
IT 9002-72-6, Growth hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(secretagogues; COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and use with other agents)

IT **52263-84-0**, (S)-Carprofen
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**)

RN 52263-84-0 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



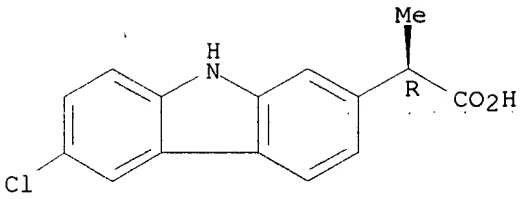
Stereo is.

IT **52263-83-9**, (R)-Carprofen
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in **dogs**, and comparative inhibition of COX-1 and -2 by carprofen and other NSAIDs)

RN 52263-83-9 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Stereois.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:129116 HCAPLUS
DOCUMENT NUMBER: 128:252467
TITLE: Enantioselectivity of the enterohepatic recycling of carprofen in the **dog**
AUTHOR(S): Priymenko, Nathalie; Garnier, Francois; Ferre, Jean -P.; Delatour, Paul; Toutain, Pierre -L.
CORPORATE SOURCE: Unite Associee INRA de Physiopathologie et Toxicologie Experimentales, Ecole Nationale Veterinaire de Toulouse, Toulouse, 31076, Fr.
SOURCE: Drug Metabolism and Disposition (1998), 26(2), 170-176
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The disposition of the two enantiomers of carprofen (CPF), the (R)-CPF and the (S)-CPF, was investigated after i.v. administration of the racemate (4 mg/kg) in **dogs** equipped with a chronic bile duct catheter. Studies in **dogs** with diverted bile flow showed that both enantiomers were extensively excreted in bile with 74% of the (R)-enantiomer and 92% of the (S)-enantiomer from the i.v. administered dose being recovered in the bile as the resp. glucuronide conjugates. The direct administration of acidic bile contg. acyl-glucuronides of CPF in the duodenum showed that both conjugated enantiomers led to high CPF enantiomer systemic availability. However, comparison of CPF pharmacokinetics between **dogs** with nondiverted bile flow and **dogs** with diverted bile flow suggested that CPF was subjected to enantioselective enterohepatic recycling (EHC) and that only the (S)-CPF was recycled. The absence of EHC for the (R)-CPF is hypothesized to be the result of formation of glucuronidase-resistant isoglucuronides (epimers) to a greater extent for the (R)-CPF than for the (S)-CPF.

CC 1-2 (Pharmacology)
IT Liver
Pharmacokinetics
(enantioselectivity of enterohepatic recycling of carprofen in **dog**)
IT Structure-activity relationship
(pharmacokinetic; enantioselectivity of enterohepatic recycling of carprofen in **dog**)
IT 53716-49-7, Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(enantioselectivity of enterohepatic recycling of carprofen in **dog**)
IT **52263-83-9**, (R)-Carprofen **52263-84-0**, (S)-Carprofen

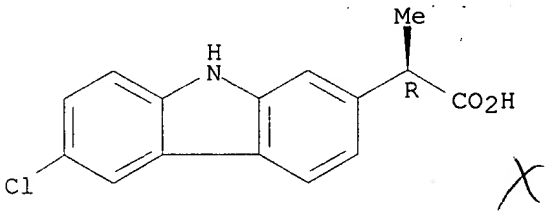
72265-94-2 72265-95-3 76319-13-6, Carprofen glucuronide
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(enantioselectivity of enterohepatic recycling of carprofen in **dog**)

IT 9001-45-0, Glucuronidase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to; enantioselectivity of enterohepatic recycling of carprofen in **dog**)

IT **52263-83-9**, (R)-Carprofen **52263-84-0**, (S)-Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(enantioselectivity of enterohepatic recycling of carprofen in **dog**)

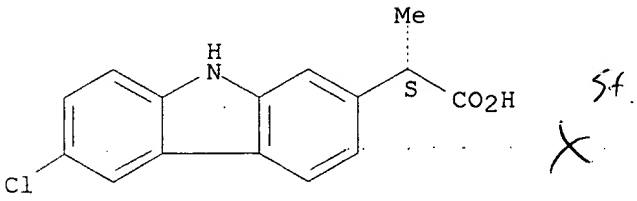
RN 52263-83-9 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 52263-84-0 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:185771 HCAPLUS
DOCUMENT NUMBER: 126:246328
TITLE: Comparative enantioselectivity in the excretion of the glucuronides of carprofen in man, **dogs** and horses
AUTHOR(S): Delatour, Paul; Garnier, Francois; Maire, Regine

CORPORATE SOURCE: Dep. Toxicol. Metabolique, Ecole Natl. Veterinaire Lyon, 69280, Fr.
SOURCE: Bulletin de l'Academie Nationale de Medecine (Paris) (1996), 180(7), 1565-1572
CODEN: BANMAC; ISSN: 0001-4079
PUBLISHER: Academie Nationale de Medecine
DOCUMENT TYPE: Journal
LANGUAGE: French

AB After administration of the racemic drug, the stereoselective quantification of the enantiomers of free and conjugated carprofen was performed in human plasma and in plasma, urine and bile of **dogs** and horses. In humans, the plasma profile of free carprofen and its glucuronides is not stereoselective and the glucuronides excreted in urine are close to a racemate. In **dogs** and horses on the contrary, the R(-) enantiomer of the free drug is predominant in plasma, while urine and/or bile concns. of the glucuronides are high in comparison to plasma with a strong selectivity for the S(+) enantiomer. Because glucuronidation of carprofen, as a carboxylic compd., is known to be the major metabolic pathway in most species, interspecies discrepancies in the stereoselective disposition of carprofen seems to be mainly related to the stereoselectivity in the excretion of the glucuronides. Finally, the high plasma concns. of carprofen glucuronides in human in comparison to other animal species suggest that the former could be specifically subjected to immunol. side effects in the time course of treatments by this type of compds.

CC 1-2 (Pharmacology)

IT Species differences
(comparative enantioselectivity in excretion of glucuronides of carprofen in man, **dogs** and horses)

IT **52263-83-9**, (-)-Carprofen **52263-84-0**, (+)-Carprofen
53716-49-7, Carprofen 72265-94-2 72265-95-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(comparative enantioselectivity in excretion of glucuronides of carprofen in man, **dogs** and horses)

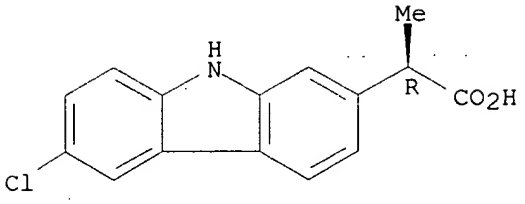
IT 76319-13-6, Carprofen glucuronide
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(comparative enantioselectivity in excretion of glucuronides of carprofen in man, **dogs** and horses)

IT **52263-83-9**, (-)-Carprofen **52263-84-0**, (+)-Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(comparative enantioselectivity in excretion of glucuronides of carprofen in man, **dogs** and horses)

RN 52263-83-9 HCAPLUS

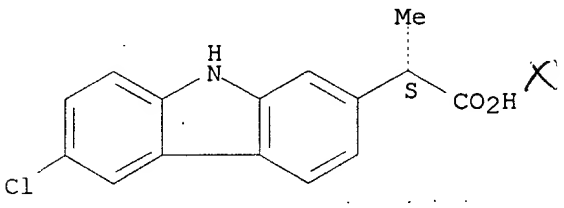
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 52263-84-0 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:368073 HCAPLUS
DOCUMENT NUMBER: 122:255754
TITLE: Stereospecific pharmacodynamics and pharmacokinetics of carprofen in the **dog**
AUTHOR(S): McKellar, Q. A.; Delatour, P.; Lees, P.
CORPORATE SOURCE: Veterinary School, University of Glasgow, Glasgow, G61 1QH, UK
SOURCE: Journal of Veterinary Pharmacology and Therapeutics (1994), 17(6), 447-54
CODEN: JVPTD9; ISSN: 0140-7783
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The non-steroidal anti-inflammatory drug (NSAID) carprofen (CPF) contains a single chiral center. It was administered orally to Beagle **dogs** as a racemate (rac-CPF) at a dose of 4 mg per kg body wt. and as individual (-)(R) and (+)(S) enantiomers at 2 mg per kg body wt. Each of the enantiomers achieved similar plasma bioavailability following administration as the racemate as they did following their sep. administration. Only the administered enantiomers were detectable when the drug was given in the (-)(R) or (+)(S) form, indicating that chiral inversion did not occur in either direction. Higher plasma concns. of the (-)(R) (Cmax 18 .mu.g/mL, AUC0-24 118 .mu.g h/mL) than the (+)(S) (Cmax 14 .mu.g/mL, AUC0-24 67 .mu.g h/mL) enantiomer were achieved following administration of the racemate. Both enantiomers distributed into peripheral s.c. tissue cage fluids, but Cmax and AUC values were lower for both transudate (non-stimulated tissue cage fluid) and exudate (induced by the intracaveal administration of the irritant carrageenan) than for plasma. Drug concns. in transudate and exudate were similar, as indicated by Cmax and AUC values, although CPF penetrated more rapidly into exudate than into transudate. Neither rac-CPF nor either enantiomer inhibited thromboxane B2 (T .times. B2) generation by platelets in clotting blood

(serum T .times. B2), or prostaglandin E2 (PGE2) and 12-hydroxyeicosatetraenoic acid (12-HETE) synthesis in inflammatory exudate. Since other studies have shown that rac-CPF at the 4 mg/kg dose rate possesses analgesic and anti-inflammatory effects in the **dog**, it is concluded that the principal mode of action of the drug must be by mechanisms other than cyclooxygenase or 12-lipoxygenase inhibition.

CC 1-7 (Pharmacology)

ST carprofen enantiomer pharmacodynamics pharmacokinetics **dog** antiinflammatory

IT **Canis familiaris**
Inflammation inhibitors
(stereospecific pharmacodynamics and pharmacokinetics of carprofen in **dog** in relation to mechanism of antiinflammatory activity)

IT 53716-49-7, Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(racemic; stereospecific pharmacodynamics and pharmacokinetics of carprofen in **dog** in relation to mechanism of antiinflammatory activity)

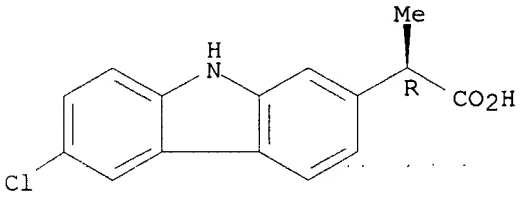
IT **52263-83-9 52263-84-0**, (S)+Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stereospecific pharmacodynamics and pharmacokinetics of carprofen in **dog** in relation to mechanism of antiinflammatory activity)

IT **52263-83-9 52263-84-0**, (S)+Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stereospecific pharmacodynamics and pharmacokinetics of carprofen in **dog** in relation to mechanism of antiinflammatory activity)

RN 52263-83-9 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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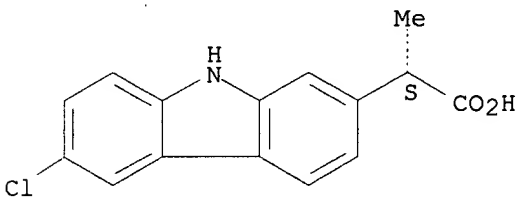
RN 52263-84-0 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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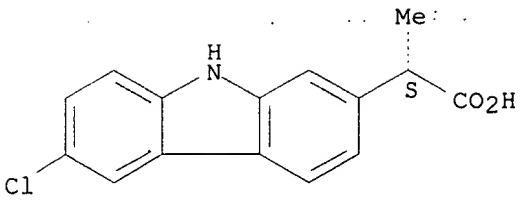
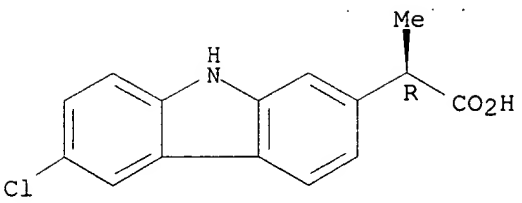


L14 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:94645 HCAPLUS
DOCUMENT NUMBER: 120:94645
TITLE: Enantioselectivity in the disposition of the nonsteroidal anti-inflammatory drugs ketoprofen and carprofen in man and animals
AUTHOR(S): Delatour, Paul; Benoit, Etienne; Bourdin, Monique; Gobron, Marc; Moysan, Frederique
CORPORATE SOURCE: Dep. Toxicol. Metab., Ec. Natl. Vet. Lyon, Marcy l'Etoile, 69280, Fr.
SOURCE: Bulletin de l'Academie Nationale de Medecine (Paris, France) (1993), 177(3), 515-27
CODEN: BANMAC; ISSN: 0001-4079
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Data are given on the pharmacokinetics of the title 2-arylpropionic acid derivs. and of their R-(-)- and S-(+)-enantiomers after administration of the racemates to humans, **dogs**, cats, sheep, dwarf pigs, dwarf goats, and horses. Considerable interspecies differences were obsd. This showed the importance of selecting an appropriate animal species when carrying out research on drugs destined for human therapy; in veterinary applications, balance must be established between the bioavailability of an active isomer and possible chiral inversion to the opposite enantiomer, with the possible generation of hybrid residues of unknown toxicity in tissues such as meat and milk.

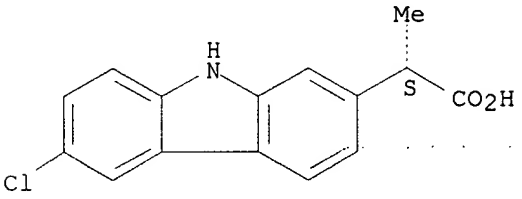
CC 1-2 (Pharmacology)
IT 22161-81-5, S-(+)-Ketoprofen **52263-83-9 52263-84-0**, S-(+)-Carprofen 56105-81-8, (-)-Ketoprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in humans and lab. animals)
IT **52263-83-9 52263-84-0**, S-(+)-Carprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in humans and lab. animals)
RN 52263-83-9 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

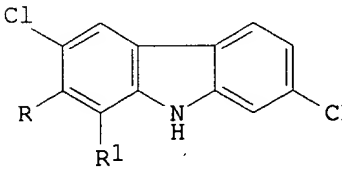


RN 52263-84-0 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:76484 HCAPLUS
DOCUMENT NUMBER: 94:76484
TITLE: Metabolism of carprofen, a nonsteroidal antiinflammatory agent, in rats, **dogs**, and humans
AUTHOR(S): Rubio, F.; Seawall, S.; Pocelinko, R.; DeBarbieri, B.; Benz, W.; Berger, L.; Morgan, L.; Pao, J.; Williams, T. H.; Koechlin, B.
CORPORATE SOURCE: Roche Res. Cent., Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE: Journal of Pharmaceutical Sciences (1980), 69(11), 1245-53
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=R1=H
II, R=OH, R1=H
III, R=H, R1=OH

AB The metabolic disposition of 14C-labeled carprofen (I) [53716-49-7] was investigated in rats, **dogs**, and humans. In **dogs** and rats, the direct conjugation of I to form an ester glucuronide [76319-13-6] and oxidn. to the C-7 (II) [**76265-33-3**] and the

C-8 (III) [**70359-64-7**] phenols followed by their conjugation represent the major metabolic pathways. Small amts. of the .alpha.-hydroxy deriv. [70359-62-5] also are formed by these species and are excreted free in the urine. In **dogs**, biliary secretion predominates, and 70% of an i.v. dose of I is excreted in the feces while 8-15% of the dose is excreted in the urine. In rats, fecal excretion due to biliary secretion varies from 60 to 75%, and urinary excretion accounts for 20-30% of an i.v. dose. In humans, direct conjugation of I represents the only significant pathway of metab. Between 65 and 70% of the orally administered I was excreted as the ester glucuronide in the urine, and most of the remaining dose was estd. to be secreted as this metabolite in the bile. Due to enterohepatic circulation, only a fraction of the biliary metabolite was recovered in the feces in humans. Less than 5% of the dose was excreted in human urine as free, intact I. In **dogs** and humans, plasma levels of I and of total radioactivity exhibit a multiphasic decline. In the human subjects studied, the terminal component declined with a 13-26-h half-life; the terminal half-life was .apprx.40 h in **dogs**.

CC 1-2 (Pharmacodynamics)

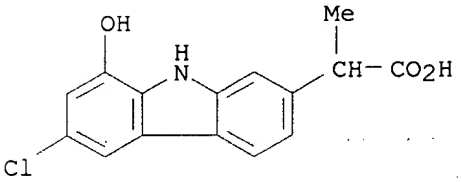
IT 70359-62-5 **70359-64-7 76265-33-3 76265-34-4 76265-35-5** 76319-13-6
RL: BIOL (Biological study)
(as carprofen metabolite, species differences in)

IT **76265-31-1P 76265-32-2P** 76265-36-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **70359-64-7 76265-33-3 76265-34-4 76265-35-5**
RL: BIOL (Biological study)
(as carprofen metabolite, species differences in)

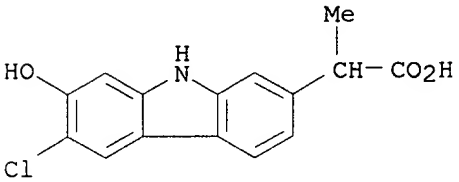
RN 70359-64-7 HCAPLUS

CN 9H-Carbazole-2-acetic acid, 6-chloro-8-hydroxy-.alpha.-methyl- (9CI) (CA INDEX NAME)



RN 76265-33-3 HCAPLUS

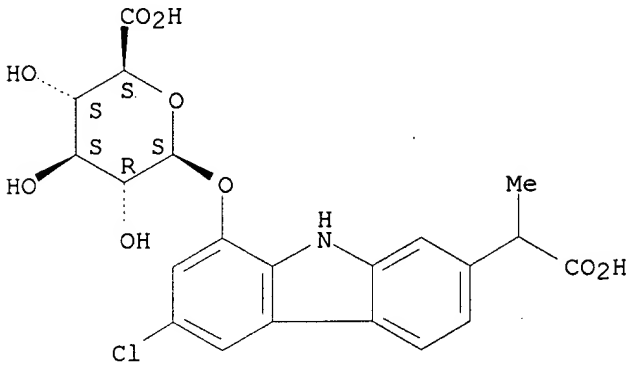
CN 9H-Carbazole-2-acetic acid, 6-chloro-7-hydroxy-.alpha.-methyl- (9CI) (CA INDEX NAME)



RN 76265-34-4 HCAPLUS

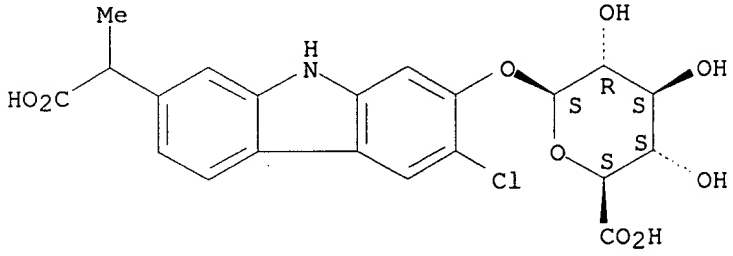
CN .beta.-D-Glucopyranosiduronic acid, 7-(1-carboxyethyl)-3-chloro-9H-carbazol-1-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

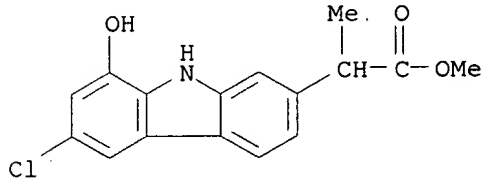


RN 76265-35-5 HCAPLUS
CN .beta.-D-Glucopyranosiduronic acid, 7-(1-carboxyethyl)-3-chloro-9H-carbazol-2-yl (9CI) (CA INDEX NAME)

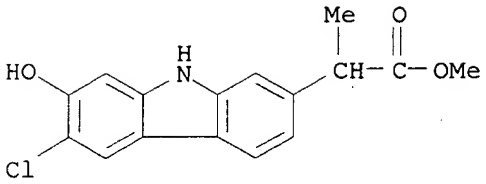
Absolute stereochemistry.



IT **76265-31-1P 76265-32-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 76265-31-1 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-8-hydroxy-.alpha.-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 76265-32-2 HCAPLUS
CN 9H-Carbazole-2-acetic acid, 6-chloro-7-hydroxy-.alpha.-methyl-, methyl ester (9CI) (CA INDEX NAME)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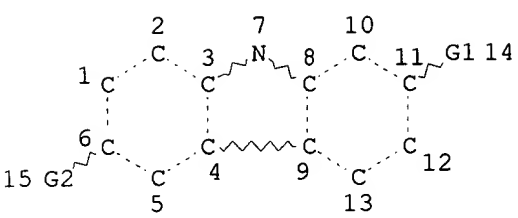

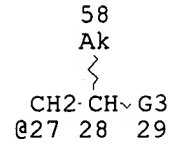

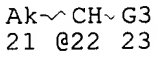

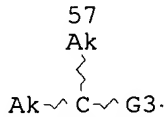

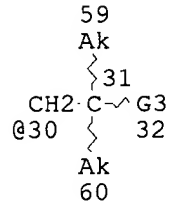

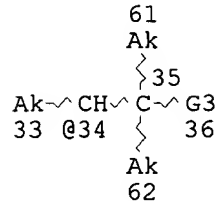

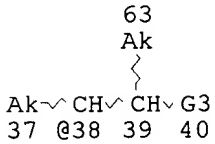

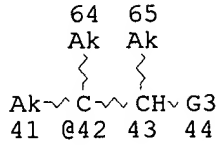

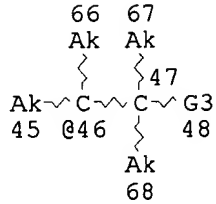

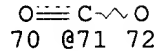

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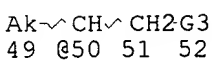
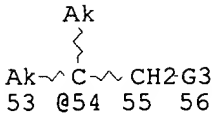
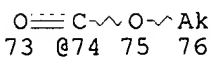
Page 1-A

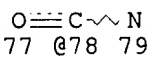
@93

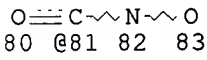
Page 1-B

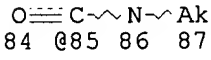


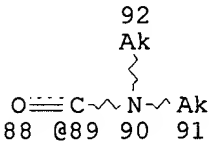


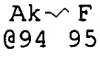












Page 2-A
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VAR G3=71/74/78/81/85/89
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CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 33

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CONNECT IS E1  RC AT  45
CONNECT IS E1  RC AT  49
CONNECT IS E1  RC AT  53
CONNECT IS E1  RC AT  57
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CONNECT IS E2  RC AT  86
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CONNECT IS E1  RC AT  93
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  95

STEREO ATTRIBUTES: NONE
L3            61 SEA FILE=REGISTRY SSS FUL L1
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CARPROFEN/CN
L8            60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L7
L17            0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L8
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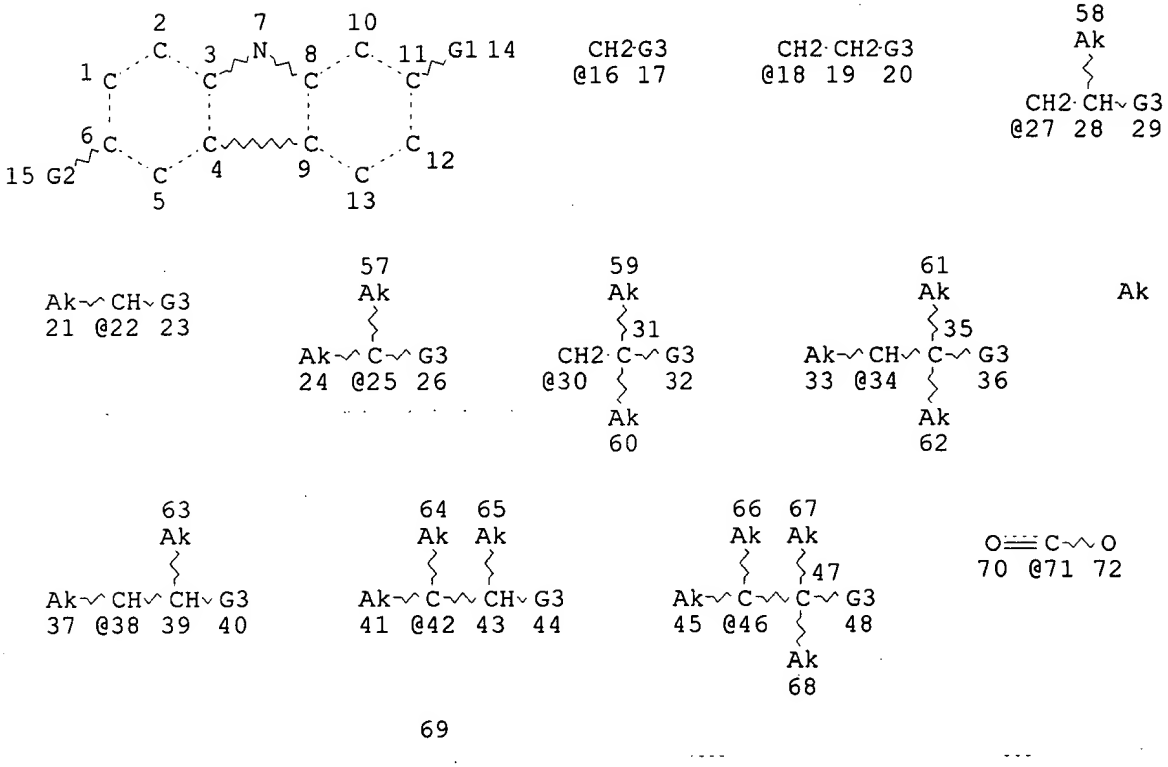
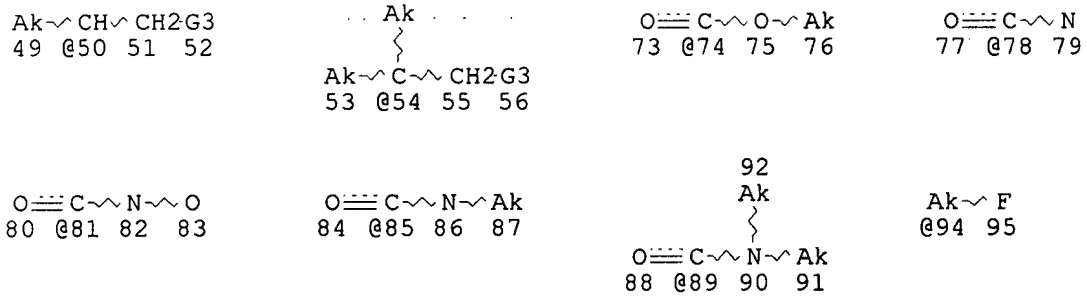


Page 1-A

@93

Page 1-B



Page 2-A
VAR G1=16/18/27/22/25/30/34/38/42/46/50/54
VAR G2=93/94/X/NO2
VAR G3=71/74/78/81/85/89
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 21
CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 33

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CONNECT IS E1  RC AT  37
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CONNECT IS E1  RC AT  93
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  95

STEREO ATTRIBUTES: NONE
L3            61 SEA FILE=REGISTRY SSS FUL L1
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CARPROFEN/CN
L8            60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L7
L18            0 SEA FILE=EMBASE ABB=ON  PLU=ON  L8
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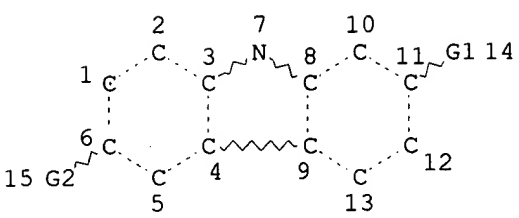
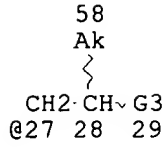
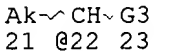
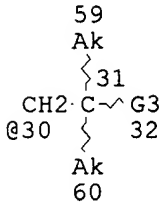
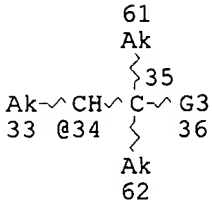
=> d que
L1 STR

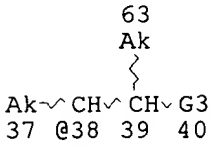


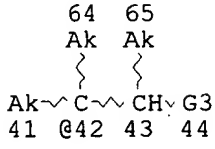


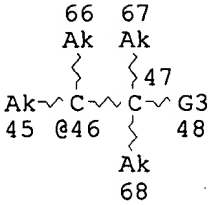


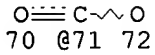












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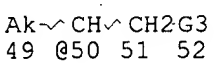

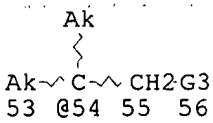

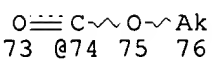

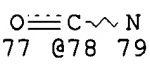

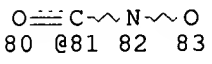

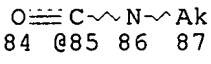

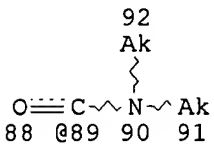

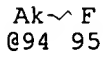

Page 2-A
VAR G1=16/18/27/22/25/30/34/38/42/46/50/54
VAR G2=93/94/X/NO2
VAR G3=71/74/78/81/85/89
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 21
CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 33

```
CONNECT IS E1  RC AT  37
CONNECT IS E1  RC AT  41
CONNECT IS E1  RC AT  45
CONNECT IS E1  RC AT  49
CONNECT IS E1  RC AT  53
CONNECT IS E1  RC AT  57
CONNECT IS E1  RC AT  58
CONNECT IS E1  RC AT  59
CONNECT IS E1  RC AT  60
CONNECT IS E1  RC AT  61
CONNECT IS E1  RC AT  62
CONNECT IS E1  RC AT  63
CONNECT IS E1  RC AT  64
CONNECT IS E1  RC AT  65
CONNECT IS E1  RC AT  66
CONNECT IS E1  RC AT  67
CONNECT IS E1  RC AT  68
CONNECT IS E1  RC AT  69
CONNECT IS E1  RC AT  72
CONNECT IS E1  RC AT  76
CONNECT IS E1  RC AT  79
CONNECT IS E1  RC AT  83
CONNECT IS E2  RC AT  86
CONNECT IS E1  RC AT  87
CONNECT IS E1  RC AT  91
CONNECT IS E1  RC AT  92
CONNECT IS E1  RC AT  93
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  95

STEREO ATTRIBUTES: NONE
L3            61 SEA FILE=REGISTRY SSS FUL L1
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CARPROFEN/CN
L8            60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L7
L9             0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L8
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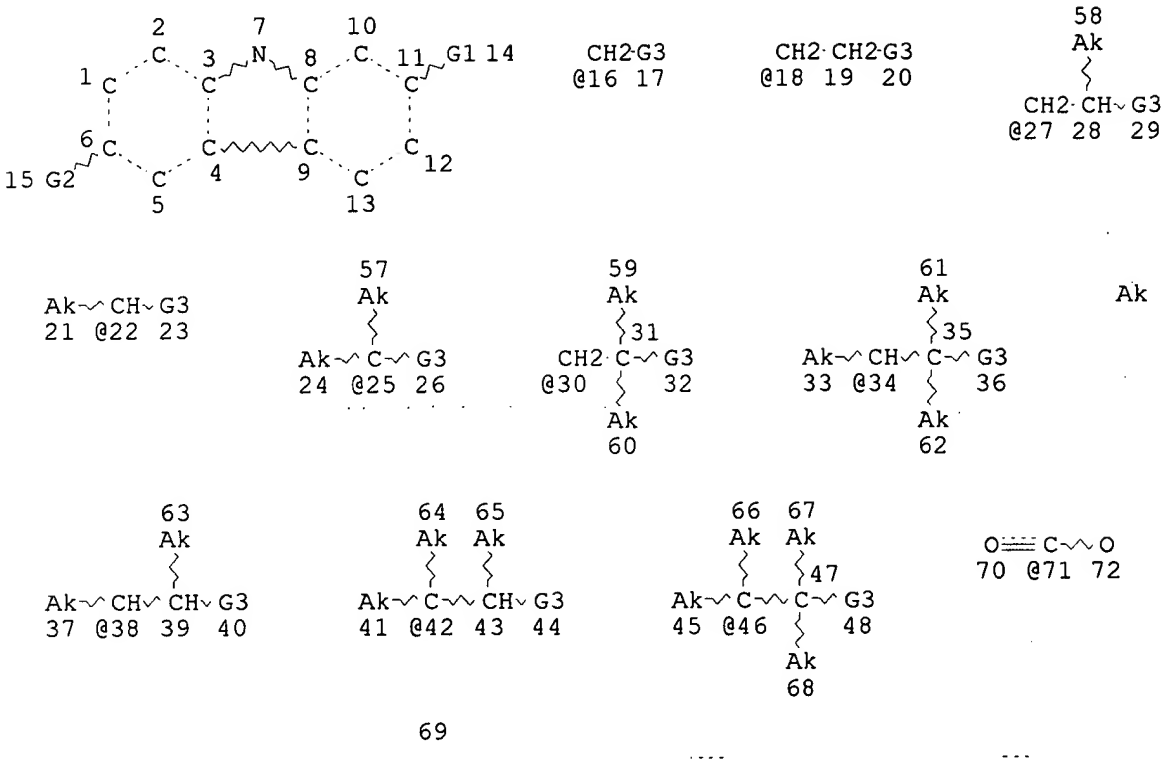
=> d que
L1 STR



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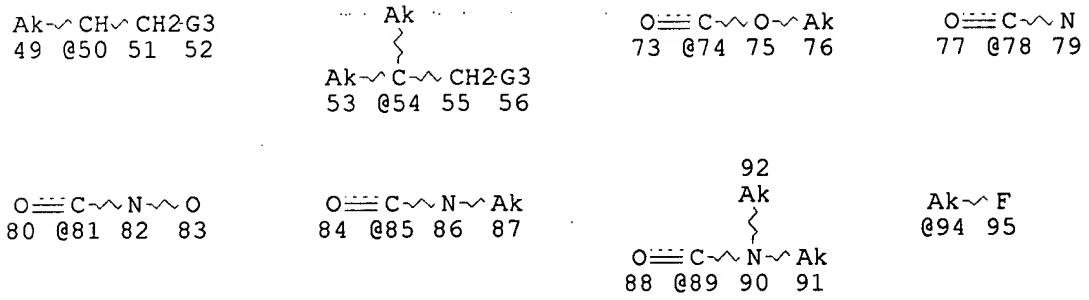

Page 2-A
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CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 33

```
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CONNECT IS E1  RC AT  41
CONNECT IS E1  RC AT  45
CONNECT IS E1  RC AT  49
CONNECT IS E1  RC AT  53
CONNECT IS E1  RC AT  57
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CONNECT IS E2  RC AT  86
CONNECT IS E1  RC AT  87
CONNECT IS E1  RC AT  91
CONNECT IS E1  RC AT  92
CONNECT IS E1  RC AT  93
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  95

STEREO ATTRIBUTES: NONE
L3            61 SEA FILE=REGISTRY SSS FUL L1
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CARPROFEN/CN
L8            60 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L7
L21            0 SEA FILE=USPATFULL ABB=ON  PLU=ON  L8 AND (DOG? OR CANI?)
```